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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,986	02/25/2005	Tadashi Nakajima	05116/HG	5004

1933 7590 01/05/2010

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EXAMINER	
BASQUILL, SEAN M	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
01/05/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,986	NAKAJIMA ET AL.	
	Examiner	Art Unit	
	Sean Basquill	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10 July 2009, 3 September 2009, and 21 October 2009 have been entered.

Status of the Claims

2. Claims 1, 2, and 21 have been amended, and Claims 3-20 and 22 have been cancelled. Claims 1, 2, and 21 are presented for examination.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1 and 2, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP/0286903A1 ("Bito"), in view of U.S. Patent 7,015,210 ("Aiken"), P. Vasantha Rao, et al, *Modulation of Aqueous Humor Outflow Facility by the Rho Kinase-Specific Inhibitor Y-27632*, 42 INV. OPHTHALMOL. VIS. SCI. 1029 (April 2001) ("Rao"), U.S. Patent 6,271,224 ("Kapin") (all of record), as put forth in the previous office actions.

Bito indicates that medical treatment of glaucoma commonly requires combination therapy owing to the fact that increased intraocular pressure (IOP) often cannot be controlled by a single therapy. (C.3, L.14-17). Bito continues on to indicate that regulating both the production and outflow of aqueous humor are effective in treating IOP, and further describe the two pathways responsible for maintaining the outflow of aqueous humor; through the trabecular meshwork and uveoscleral routes. (C.2, L.37-49). Bito also indicates that prostaglandin derivatives reduce IOP by increasing uveoscleral outflow. C.1, L.48-50). Bito neither specifically recites any of the claimed prostaglandins, nor specifies rho-kinase inhibitors as effective combination therapeutics.

Aiken echoes the Bito insistence on the use of combination therapy including prostaglandins in the treatment of IOP. (C.9, L.66-C.10, L.11) Aiken further indicates that prostaglandins such as latanoprost, unoprostone isopropyl, and travaprost, among others, which are known to treat IOP can also be used as part of combination therapy when paired with a compound or drug which operates through a distinct mechanism of action. (C.10, L.2-7, 19-31). Aiken, like Bito, prefers combination therapies utilizing both an outflow enhancing agent and an aqueous humor production reducing agent, here an epoxy-steroidal aldosterone receptor antagonist (C.10, L.1—26), but emphasizes that complementary mechanisms of action are the primary concern (c.10, L.7-11).

Rao indicates that the rho-kinase inhibitor Y-27632 ([(+)-R-trans-4-(1-aminoethyl)-*N*-(4-pyridyl) cyclohexanecarboxamide] (Rao *at* 1030), appear to improve aqueous outflow through the trabecular meshwork (Schlemm's canal). (*Id. at* 1034).

Kapin indicates isoquinoline compounds, preferably 1-(5-isoquinolinesulfonyl)-homopiperazine as well as pharmaceutically acceptable salts thereof, are effective in lowering IOP. (C.2, L.31-33; C.3, L.19-24). A preferred embodiment of the invention of Kapin uses the hydrochloride salt of 1-(5-isoquinolinesulfonyl)-homopiperazine, commonly known as FASUDIL.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time of the instant invention to have combined a prostaglandin such as latanoprost with a rho kinase inhibitor such as the hydrochloride salt of 1-(5-isoquinolinesulfonyl)-homopiperazine to form a composition which contains two compounds known to treat the same disease, in this case glaucoma. One having ordinary skill in the art would have been motivated to do so because it is well established, binding legal precedent which commands a finding of obviousness where two elements known to be useful for the same purpose are combined to provide a third composition useful for the exact purpose for which the individual components are known to demonstrate utility. The idea for combining them flows logically from their having been individually taught in the prior art. MPEP 2144.06.

Applicants arguments have been fully considered and are deemed unpersuasive. Applicants are reminded that in formulating an obviousness rejection under 35 USC 103, it is unnecessary, in fact contrary to the intent and meaning of the statute, to have one prior art reference teach each and every element of the invention as claimed by the applicants. An obviousness rejection requires nothing more than the examiner's demonstration that each of the elements claimed by the applicants were known in the prior art, and articulate some reasoning with a rational underpinning to support the legal conclusion of obviousness flowing therefrom.

KSR International Co. v. Teleflex, Inc., 82 USPQ2d 1385, 1396 (U.S. 2007). Moreover, "[w]hen a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious." *Id.* at 1395 (quoting *Sakraida v. A.G. Pro*, 425 U.S. 273, 282 (1976)). "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious," the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." (*Id.*).

To effectively rebut such a *prima facie* case of obviousness, applicants' only recourse is to demonstrate, by the filing of a properly executed declaration or affidavit compliant with 37 CFR 1.132 containing sufficient evidence of secondary indicia of nonobviousness commensurate in scope with the invention as claimed. MPEP 2145. Applicants arguments neither comply with this requirement nor provide sufficient evidence demonstrating that the results obtained by the claimed combination are in fact unexpected. As indicated in previous office actions, both Bito and Aiken specifically advocate the use of prostaglandins in combination therapy for the treatment of glaucoma owing to the improvement in lowering of intraocular pressure obtained by administration of such combination therapy. Any distinction applicants have demonstrated in comparing the combination of, for example, latanoprost and the hydrochloride salt of 1-(5-isoquinolinesulfonyl)-homopiperazine is therefore expected by the skilled artisan. Unless and until applicants properly provide sufficient evidence to clearly demonstrate that the IOP lowering results obtained by the combination of, for example, the combination of latanoprost and the hydrochloride salt of 1-(5-isoquinolinesulfonyl)-homopiperazine is unexpected to the skilled artisan, the rejections of record will stand.

Conclusion

No Claims are allowable

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean Basquill whose telephone number is (571) 270-5862. The examiner can normally be reached on Monday through Thursday, between 8AM and 6PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sean Basquill
Art Unit 1612

/JEFFREY S. LUNDGREN/
Primary Examiner, Art Unit 1639